REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 52-101 are pending in the application. Claims 53-58, 62, 64-68, 92-94 and 95-101 are withdrawn from consideration pursuant to an election of species. At least claims 52 and 63 generic. Claims 52, 59-61, 63, 69-91 and 95 are under consideration and stand rejected.

Claim 102 has been added. Support for claim 102 can be found in the claims as originally filed.

No new matter has been added.

35 U.S.C. § 112, first paragraph

Claims 52-59-61, 63, 69-91 and 95 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to enable a person of skill in the art to make and/or use the claimed invention. The allegation has been traversed.

The Examiner has copied allegations from prior Office Actions to the effect that "Attempts to induce tolerance in humans have been completely unsuccessful in at least two documented instances." The Examiner refers to two trials as "complete failure[s]." As evidence, the Examiner refers to a blurb in the trade publication *Marketletter.*

The "evidence" cited by the Examiner is nowhere near being proof of "complete failure." The *Marketletter* article does not state that testing of Colloral was stopped because it was harmful or because the treatment had no effect. The *Marketletter* reports that the statistical results did not warrant further spending on late clinical trials. The *Marketletter* is reporting a business decision, based on insufficient statistical results and financial considerations, not a scientific conclusion, and not a determination of effectiveness by the FDA. Moreover, whether a treatment has passed regulatory hurdles is irrelevant. The Federal Circuit has cautioned the PTO not to "confuse[] the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption." *In re Brana*, 34 USPQ2d 1437, 1442 (Fed. Cir. 1995).

The Examiner has also relied upon Goodnow, *The Lancet*, 357:2115-20, 2001. Goodnow states on page 2118 that a phenomenon of oral tolerance exists and that clinical trials are underway involving the induction of oral tolerance. Goodnow does not support an allegation that oral tolerance does not work. Goodnow nether provides nor cites empirical data refuting that oral tolerance is achievable. Rather, Goodnow supports the proposition that oral tolerance is achievable.

Applicants have provided extensive evidence in the past that oral tolerance methods have been found to be effective in a variety of contexts. Applicants now provide the following additional evidence: Womer et al., *Clinical Transplantation*, 22:754-9, 2008 stated, we demonstrate complete suppression of baseline indirect alloreactivity in patients with chronic renal allograft dysfunction. The authors concluded that oral feeding of low dose donor MHC

peptide may present a safe and effective therapy to suppress indirect alloreactivity in renal transplant patients. (Exhibit A)

Thus, it is clear that oral tolerance has been shown to be a viable method of treating allograft rejection in transplant patients and in many other contexts. The Examiner has discounted each piece of evidence that has been presented in the past. However, it is respectfully submitted that the overwhelming weight of the evidence taken as a whole demonstrates that there is no basis for the contention that the methods described in the specification are not enabled. The phenomenon that underlies the invention has been demonstrated repeatedly in a wide variety of applications, including the elected species.

Accordingly, withdrawal of the rejection is respectfully requested.

35 U.S.C. § 103

Claims 52, 59-61, 63, 69-91 and 95 have been rejected under 35 U.S.C. § 103 as allegedly unpatentable over PCT published application WO 92/07581 in view of U.S. Patent No. 5,484,719 ("the '719 patent").

The cited art does not teach every element of the claimed invention. Nowhere in the WO 92/07581 publication is it suggested that oral administration of a transgenic plant is an alternative method of suppressing an immune response. The '719 patent also fails to disclose oral administration of plants for suppression of an immune response.

Moreover, the proposed combination of the references is per se non-obvious under the law. The objectives of the two references are diametrically opposed and combining the references as proposed would change the principle of operation of the '719 patent. Indeed, the

objective of the '719 patent is the opposite of the objective of the present application. The '719 patent teaches that expression of antigens from viral, bacterial or fungal antigens in a plant for a method of oral vaccination will have the effect of increasing the immune response. The present application is directed to the induction of oral tolerance with tolerogenic antigens with the object of suppressing an immune response.

The Office has contended that "sound scientific reasoning" would lead one of ordinary skill in the art to believe that if viral, bacterial, and fungal antigens could be produced in a plant, then so could tolerogenic antigens. However, if the references were combined, the expected result could only be the opposite of the effect sought by the present invention.

In such a case, the black-letter law is clear. If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984). If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 U.S.P.Q. 349 (CCPA 1959).

Moreover, applicants have presented evidence of secondary indicia of non-obviousness. The Examiner discounts the recognition of Dr. Jevnikar's contribution as not addressing the specific invention. Applicants respectfully point out that the report of the award specifically refers to Dr. Jevnikar's "Novel expression and drug delivery systems for topical and oral delivery of proteins that modulate the body's immune response." Applicants respectfully submit

that that is recognition in the art of the novelty of Dr. Jevnikar's contributions in the subject matter of the invention.

For at least these reasons, withdrawal of the rejection remains appropriate.

Obviousness-type double patenting rejection

The remaining rejections under the judicially created doctrine of obviousness-type double patenting are provisional and will be addressed in the event that the rejections are rendered non-provisional.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: February 3, 2009

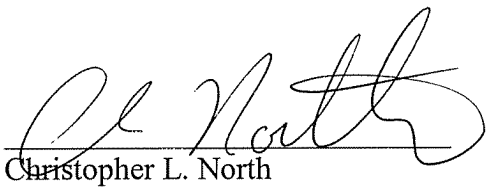
By: 

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EXHIBIT A

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Search **"Clinical transplantation"[Jour] AND 22[volume] AND 754[page] AND 2008[pdat]**

1: Clin Transplant. 2008 Nov-Dec;22(6):754-9. Epub 2008 Jul 18.

FULL TEXT AVAILABLE ONLINE WILEY InterScience

A pilot study on the immunological effects of oral administration of donor major histocompatibility complex class II peptides in renal transplant recipients.

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Oral tolerance is an important physiological mechanism of immune hyporesponsiveness to dietary antigens and the commensal flora of the gastrointestinal tract. Feeding of alloantigens, therefore, has the potential to suppress undesirable immune responses after transplantation. To date, there are no published reports on the effects of such an approach in human transplant recipients. In the present pilot study, we demonstrate complete suppression of baseline indirect alloreactivity in patients with chronic renal allograft dysfunction following the oral feeding of low (0.5 mg/d) but not higher (1.0 and 5.0 mg/d) doses of donor major histocompatibility complex (MHC) class II peptides. The regimen was well tolerated with no evidence for sensitization to the donor antigen. Our results indicate that oral feeding of low dose donor MHC peptide may represent a safe and effective therapy to suppress indirect alloreactivity in renal transplant recipients with chronic allograft dysfunction and warrants further clinical investigation.

Publication Types:
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